so that the polynucleotide could be packaged into a rAAV. Analogously, Rich et al. (1991, Science **253**: 205-207) described a CFTR derivative missing amino acid residues 708-835, that was capable of transporting chloride and capable of correcting a naturally occurring CFTR defect. To take two additional examples, Arispe et al. (1992, Proc. Natl. Acad. Sci. USA **89**: 1539-1543) showed that a CFTR fragment comprising residues 433-586 was sufficient to reconstitute a correct chloride channel in lipid bilayers; and Sheppard et al. (1994, Cell **76**: 1091-1098) showed that a CFTR polypeptide truncated at residue 836 to about half its length was still capable of building a regulated chloride channel. Thus, the native CFTR protein, and mutants and fragments thereof, all constitute CFTR polypeptides that are useful under this invention.

In the claims

Please cancel claims 1-35 without prejudice or disclaimer.

Please add new claims 36-99 as follows:

36. (New) A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and one or more heterologous transcriptionally active elements incorporated 3' with respect to the ITR, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the one or more heterologous transcriptionally active elements under conditions permissive for transcription, wherein at least one of the one or more heterologous transcriptionally active elements is a human transcriptionally active element, and wherein the region is less than about 400 bp in length.

37. (New) A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 200 bp.

38. (New) A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about seven-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

39. (New) A polynucleotide according to claim 38 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a transcription initiator sequence and at least one CCAC box.

40. (New) A polynucleotide according to claim 39 wherein the transcription initiator sequence and at least one CCAC box are contained within a polynucleotide segment less than about 90 nt.

41. (New) A polynucleotide according to claim 40 wherein the one or more transcriptionally active elements have at least about 90% overall identity to SEQ ID NO:17, or the sequence complementary thereto.

42. (New) A polynucleotide according to claim 39 wherein said polynucleotide comprises SEQ ID NO:17.

43. (New) A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 10-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

44. (New) A polynucleotide according to claim 43 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a transcriptionally active element of an amyloid β-protein precursor (APP) promoter and a transcription initiator sequence.

45. (New) A polynucleotide according to claim 44 wherein the transcriptionally active element of an amyloid β-protein precursor (APP) promoter and the transcription initiator sequence are contained within a polynucleotide segment less than about 70 nt.

46. (New) A polynucleotide according to claim 45 wherein the transcriptionally active element has at least about 90% overall sequence identity to SEQ ID NO:7, or the sequence complementary thereto.

47. (New) A polynucleotide according to claim 44 wherein said polynucleotide comprises SEQ ID NO:7.

48. A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 40-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

49. (New) A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 50-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

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50. (New) A polynucleotide according to claim 36 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

51. (New) A polynucleotide of claim 50, wherein the gene is a CFTR gene.

52. (New) A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally

active elements, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific, and wherein the heterologous segment has a deletion compared to its native sequence.

53. (New) A polynucleotide according to claim 52 wherein the heterologous segment is less than 200 nucleotides.

54. (New) A polynucleotide according to claim 52 wherein the heterologous segment is less than 100 nucleotides.

55. (New) A polynucleotide according to claim 52 wherein at least one of the transcriptionally active elements is tissue specific.

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56. (New) A polynucleotide according to claim 52 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

57. (New) A polynucleotide of claim 56, wherein the gene is a CFTR gene.

58. (New) A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements which are removed from a promoter, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, and wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific.

59. (New) A polynucleotide according to claim 58 wherein the heterologous segment is less than 200 nucleotides.

60. (New) A polynucleotide according to claim 58 wherein the heterologous segment is less than 100 nucleotides.

61. (New) A polynucleotide according to claim 58 wherein at least one of the transcriptionally active elements is tissue specific.

62. (New) A polynucleotide according to claim 58 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

63. (New) A polynucleotide of claim 62, wherein the gene is a CFTR gene.

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64. (New) A polynucleotide comprising, in order:

a region containing a first AAV ITR and one or more heterologous transcriptionally active elements incorporated 3' with respect to the ITR, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription, wherein at least one of the one or more heterologous transcriptionally active elements is a human transcriptionally active element, and wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 400 bp in length; and

a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

65. (New) A polynucleotide according to claim 64 wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 200 bp.

66. (New) A polynucleotide according to claim 64 further comprising a gene operably linked to the region containing the ITR and the one or more heterologous transcriptionally active elements.

67. (New) A polynucleotide according to claim 66, wherein the gene is a CFTR gene.

68. (New) A plasmid comprising a polynucleotide of claim 64, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

69. (New) An AAV viral particle comprising a polynucleotide of claim 64.

70. (New) An AAV viral particle according to claim 69, wherein the polynucleotide is between 4.6 kb and 5.0 kb in length.

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71. (New) A polynucleotide comprising, in order:

a region containing a first AAV ITR and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements, wherein the transcriptional activity is increased at least two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific, and wherein the heterologous segment has a deletion compared to its native sequence; and

a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

72. (New) A polynucleotide of claim 71, wherein the starting site of the first AAV ITR and the ending site of the second AAV ITR are contained within a polynucleotide segment between 4.6 kb and 5.0 kb in length.

73. (New) A polynucleotide of claim 71, wherein the heterologous segment is less than 200 nucleotides.

74. (New) A polynucleotide of claim 71, wherein at least one of the transcriptionally active elements is tissue specific.

75. (New) A polynucleotide of claim 71, further comprising a gene operably linked to the region containing the ITR and the heterologous segment.

76. (New) A polynucleotide of claim 75, wherein the gene is a CFTR gene.

77. (New) A plasmid comprising a polynucleotide of claim 71, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

78. (New) An AAV viral particle comprising a polynucleotide of claim 71.

79. (New) An AAV viral particle according to claim 78, wherein the polynucleotide is between 4.6 and 5.0 kb in length.

80. (New) A polynucleotide comprising, in order:

a region containing a first AAV ITR and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more

transcriptionally active elements which are removed from a promoter, wherein the transcriptional activity is increased at least two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, and wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific; and

a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

81. (New) A polynucleotide of claim 80, wherein the starting site of the first AAV ITR and the ending site of the second AAV ITR are contained within a polynucleotide segment between 4.6 kb and 5.0 kb in length.

82. (New) A polynucleotide of claim 80, wherein the heterologous segment is less than 200 nucleotides.

83. (New) A polynucleotide of claim 80, wherein at least one of the transcriptionally active elements is tissue specific.

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84. (New) A polynucleotide of claim 80, further comprising a gene operably linked to the region containing the ITR and the heterologous segment.

85. (New) A polynucleotide of claim 84, wherein the gene is a CFTR gene.

86. (New) A plasmid comprising a polynucleotide of claim 80, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

87. (New) An AAV viral particle comprising a polynucleotide of claim 80.

88. (New) An AAV viral particle according to claim 87, wherein the polynucleotide is between 4.6 and 5.0 kb in length.

89. (New) A mammalian cell comprising a polynucleotide according to claim 36, wherein said polynucleotide is stably integrated into a chromosome of said cell.

90. (New) A mammalian cell of claim 89, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

91. (New) A mammalian cell of claim 89, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

92. (New) A mammalian cell comprising a polynucleotide according to claim 52, wherein said polynucleotide is stably integrated into a chromosome of said cell.

93. (New) A mammalian cell of claim 92, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

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94. (New) A mammalian cell of claim 92, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

95. (New) A mammalian cell comprising a polynucleotide according to claim 58, wherein said polynucleotide is stably integrated into a chromosome of said cell.

96. (New) A mammalian cell of claim 95, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

97. (New) A mammalian cell of claim 95, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

98. (New) A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a heterologous transcription initiator sequence.

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99. (New) A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a TATA box as a transcription initiator sequence.